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L34 ANSWER 1 OF 17 MEDLINE
AN **1999086764** MEDLINE
DN **99086764** PubMed ID: **9869940**
TI Experience with **pancreas islets** separation, immunoisolation and cryopreservation.
AU Orlowski T; Tatarkiewicz K; Sitarek E; Sabat M; Fiedor P; Samsel R
CS Transplantation Institute, Warsaw Medical School, Poland.
SO ANNALS OF TRANSPLANTATION, **(1996)** 1 (1) 54-8.
Journal code: 9802544. ISSN: 1425-9524.
CY Poland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199901
ED Entered STN: 19990202
Last Updated on STN: 19990202
Entered Medline: 19990119
AB Experience of Warsaw **Pancreas** Laboratory is presented. Some improvement in the methods of rat, human and pig **pancreases** digestion, and in identification of **Langerhans islets** by means of intravenous injection of I-DTZ was achieved. For immunoisolation of **islets**, 2 methods were elaborated: capsules containing alginate/polyethyleneimine/protamine/**heparin** membrane prepared by modified Sun method, and microcapsules based on Zekorn method. Biocompability of hollow fibers, prepared with polypropylene (PP), surface modified PP (PPS) and polysulphone (PS) was assessed in vitro. Only PS fibers were fully compatible. It was shown, that the mixture of exocrine tissue did not influence in vitro insulin secretion, providing that alginate in which **islets** are embedded remain gelled. The efficacy of 3 methods of **islets** cryopreservation was compared: freezing in "semicontrolable" conditions, in programmable Kriomedpol machine, and vitrification. The highest percentage of frozen/thawed living cells, and the most reliable results were obtained with Kriomedpol method.

CT Check Tags: Animal; Human
Alginates
Biocompatible Materials
Capsules
Cell Culture: MT, methods
Cell Separation: MT, methods
Cells, Cultured
*Cryopreservation: MT, methods
*Diabetes Mellitus, Experimental: SU, surgery
Heparin
Indicators and Reagents
Insulin: SE, secretion
***Islets of Langerhans**
Islets of Langerhans: CY, cytology
Islets of Langerhans: SE, secretion
Mice
Polyethyleneimine
Polymers
Polypropylenes
Protamines
Rats
Sulfones
Swine
Time Factors
Transplantation, Heterologous
RN 11061-68-0 (Insulin); 25135-51-7 (polysulfone P 1700); 9002-98-6 (Polyethyleneimine); 9005-32-7 (alginic acid); **9005-49-6 (Heparin)**
CN 0 (Alginates); 0 (Biocompatible Materials); 0 (Capsules); 0 (Indicators and Reagents); 0 (Polymers); 0 (Polypropylenes); 0 (Protamines); 0 (Sulfones)

L34 ANSWER 2 OF 17 MEDLINE
AN **1998165631** MEDLINE
DN **98165631** PubMed ID: **9506786**
TI Comparison of two methods of **pancreas islets** immunoisolation.
AU Orlowski T; Sitarek E; Tatarkiewicz K; Sabat M; Antosiak M
CS Transplantation Institute, Warsaw School of Medicine, Warszawa, Poland.
SO INTERNATIONAL JOURNAL OF ARTIFICIAL ORGANS, **(1997 Dec)** 20 (12) 701-3.
Journal code: 7802649. ISSN: 0391-3988.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199805
ED Entered STN: 19980520
Last Updated on STN: 19990129
Entered Medline: 19980514
AB The efficacy of two methods of **Langerhans islets** immunoisolation was compared. For this purpose the function of **islets** encapsulated with alginate/polyethylenimine/protamine/ **heparin** (APPH) or with alginate/poly-L-lisine/alginate (APA) membranes was assessed: in vitro according to their survival and response to glucose challenges, and in vivo according to their capability to provide sufficient insulin delivery to maintain normal fasting blood glucose following xenotransplantation to streptozotocin diabetic mice. In vitro insulin secretion and the response to glucose challenge of APPH and APA encapsulated **islets** were comparable to free **islets** . In vivo intraperitoneal concordant xenotransplantation of APA encapsulated rat **islets** reversed the diabetic state of streptozotocin diabetic mice for a longer period, than APPH **islet** grafts. This study clearly demonstrated the inadequacy of in vitro methods

in the prediction of in vivo results of **islets** transplantation.

CT Check Tags: Animal; Comparative Study; Male; Support, Non-U.S. Gov't
Alginates
Biocompatible Materials
Blood Glucose: AN, analysis
Diabetes Mellitus, Experimental: BL, blood
Diabetes Mellitus, Experimental: SU, surgery
*Diabetes Mellitus, Experimental: TH, therapy
Glucose: DU, diagnostic use
Insulin: SE, secretion
Islets of Langerhans: SE, secretion
Islets of Langerhans Transplantation: IM, immunology
***Islets of Langerhans Transplantation: MT, methods**
*Membranes, Artificial
Mice
Mice, Inbred BALB C
Pancreas, Artificial
Polylysine: AA, analogs & derivatives
Rats
Tissue Culture
Transplantation, Heterologous

RN 11061-68-0 (Insulin); 25104-18-1 (Polylysine); 50-99-7 (Glucose)

CN 0 (Alginates); 0 (Biocompatible Materials); 0 (Blood Glucose); 0 (alginate-polylysine-alginate)

L34 ANSWER 3 OF 17 MEDLINE

AN **97438103** MEDLINE

DN **97438103** PubMed ID: **9293878**

TI Expansion of intermediate T cell receptor cells expressing interleukin-2 receptor alpha- beta+, CD8alpha+ beta+, and lymphocyte function-associated antigen-1+ in the liver in association with intrahepatic islet xenograft rejection from rat to mouse: prevention of rejection with anti-interleukin-2 receptor beta **monoclonal antibody** treatment.

AU Ohtsuka K; Yasunami Y; Ikehara Y; Nagai T; Kodama S; Maki T; Tomita A; Abo T; Ikeda S

CS Department of Surgery I, Fukuoka University School of Medicine, Japan.

SO TRANSPLANTATION, **(1997 Aug 27)** 64 (4) 633-9.
Journal code: 0132144. ISSN: 0041-1337.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199709

ED Entered STN: 19971013
Last Updated on STN: 19971013
Entered Medline: 19970930

AB BACKGROUND: The precise mechanisms involved in islet xenograft rejection remain unknown. The purpose of the present study was to determine cellular mechanisms responsible for islet xenograft rejection in the liver to facilitate finding a procedure for prevention of immune rejection. METHODS: Hepatic mononuclear cells (MNC) as well as splenocytes, peripheral blood MNC, and thymocytes from streptozotocin-induced diabetic mice (BALB/c) rejecting the intrahepatic rat (Lewis) islet xenografts were isolated and examined by two-color FACS analysis. RESULTS: The characteristic finding of the hepatic MNC from the mice rejecting islet xenografts compared with mice receiving isografts was a significant increase in the yield as well as in the percentage of the cells expressing CD3+ interleukin-2 receptor (IL-2R) alpha- beta+, CD3+ CD8alpha+ beta+, and T cell receptor (TCR) alphabeta+ lymphocyte function-associated antigen-1+. The expression of CD3 and TCR alphabeta of these T cells was found to be of intermediate intensity (TCR(int) cells). The expansion of these TCR(int) cells occurred predominantly in the liver. There was no

significant difference in the cells expressing CD3+ IL-2R alpha+, CD3+ CD4+, CD3+ TCRgammadelta+, CD3- IL-2Rbeta+ (natural killer cells), and B220+ (B cells). In vivo administration of anti-IL-2Rbeta **monoclonal antibody** directed to the expanded cells produced a prevention of rejection. CONCLUSIONS: These findings suggest that islet xenograft rejection in the liver from rat to mouse is an event for which the TCR(int) cells are responsible.

CT Check Tags: Animal; Support, Non-U.S. Gov't
Antibodies, Monoclonal: TU, therapeutic use
Antigens, CD3: BI, biosynthesis
Flow Cytometry
Graft Rejection: PC, prevention & control
Graft Survival: DE, drug effects
***Islets of Langerhans Transplantation: IM, immunology**
Leukocytes, Mononuclear: CY, cytology
*Liver: CH, chemistry
Liver: CY, cytology
Liver: SU, surgery
***Lymphocyte Function-Associated Antigen-1: AN, analysis**
Mice
Mice, Inbred BALB C
Monocytes: CY, cytology
Rats
Rats, Inbred Lew
*Receptors, Antigen, T-Cell, alpha-beta: AN, analysis
*Receptors, Interleukin-2: IM, immunology
Spleen: CY, cytology
T-Lymphocytes: CY, cytology
Thymus Gland: CY, cytology
***Transplantation, Heterologous: IM, immunology**

CN 0 (**Antibodies, Monoclonal**); 0 (Antigens, CD3); 0 (Lymphocyte Function-Associated Antigen-1); 0 (Receptors, Antigen, T-Cell, alpha-beta); 0 (Receptors, Interleukin-2)

L34 ANSWER 4 OF 17 MEDLINE
AN **95363081** MEDLINE
DN **95363081** PubMed ID: **7543517**
TI Ex vivo coating of islet cell allografts with murine CTLA4/**Fc** promotes graft tolerance.
AU Steurer W; Nickerson P W; Steele A W; Steiger J; Zheng X X; Strom T B
CS Harvard Medical School, Department of Medicine, Boston, MA, USA.
SO JOURNAL OF IMMUNOLOGY, **(1995 Aug 1)** 155 (3) 1165-74.
Journal code: 2985117R. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199509
ED Entered STN: 19950921
Last Updated on STN: 19960129
Entered Medline: 19950912
AB To test the hypothesis that blockade of B7-triggered costimulation by donor cells could preclude allograft rejection, we coated crude islet allograft preparations in vitro for 1 h with a murine CTLA4/**Fc** fusion protein. Murine CTLA4/**Fc** blocks the proliferative response in primary mixed lymphocyte cultures (MLC) and Con A-stimulated murine spleen cell cultures by 85 to 95%. Responder cells from a primary MLC containing mCTLA4/**Fc** were hyporesponsive upon restimulation to the same stimulator cells in a secondary MLC lacking mCTLA4/**Fc** . Because of mutations in the **Fc** gamma RI and C'1q binding sites of the **Fc** portion of the murine CTLA4/**Fc** fusion protein, the molecule binds to, but does not target, cells for Ab-dependent cellular cytotoxicity or complement-directed cytolysis.

Although systemic immunosuppression was not applied, 42% (10 of 24) of B6AF1 recipients of islet allografts pretreated with CTLA4/**Fc** were permanently engrafted. Further, 50% of hosts bearing functioning islet allografts more than 150 days post-transplant were formally proved to be tolerant to donor tissues. A persistent CD4+ and CD8+ T cell infiltrate surrounding, but not invading, islet grafts in tolerant hosts was discerned. In control experiments, 89% (8 of 9) of islet allografts coated with mIgG3, and 100% (n = 10) pretreated with media alone were rejected. Thus, we conclude that 1) B7-triggered costimulation by donor APCs is an important element of rejection, and 2) blockade of the B7 pathway by in vitro allograft manipulation is able to induce tolerance.

CT Check Tags: Animal; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Antigen-Presenting Cells: IM, immunology
Antigens, CD28: IM, immunology
Antigens, CD80: PH, physiology
Antigens, Differentiation: GE, genetics
*Antigens, Differentiation: PD, pharmacology
CHO Cells
Cell Line
Concanavalin A: PD, pharmacology
*Graft Enhancement, Immunologic
Graft Rejection: PC, prevention & control
Graft Survival: DE, drug effects
Graft Survival: IM, immunology
Hamsters
Immune Tolerance
Immunoglobulins, Fc: GE, genetics
***Immunoglobulins, Fc: PD, pharmacology**
***Islets of Langerhans Transplantation**
Lymphocyte Culture Test, Mixed
Lymphocyte Transformation: DE, drug effects
Mice
Mice, Inbred Strains
Mutagenesis, Site-Directed
Receptors, IgG: ME, metabolism
*Recombinant Fusion Proteins: PD, pharmacology

RN 11028-71-0 (Concanavalin A)

CN 0 (Antigens, CD28); 0 (Antigens, CD80); 0 (Antigens, Differentiation); 0 (CTLA-4); 0 (Immunoglobulins, **Fc**); 0 (Receptors, IgG); 0 (Recombinant Fusion Proteins)

L34 ANSWER 5 OF 17 MEDLINE

AN **95350844** MEDLINE

DN **95350844** PubMed ID: **7624946**

TI Prolongation of rat islet allograft survival by treatment with **monoclonal antibodies** against VLA-4 and LFA-1.

AU Yang H; Issekutz T B; Wright J R Jr

CS Department of Pathology, Izaak Walton Killam Children's Hospital, Dalhousie University Faculty of Medicine, Halifax, Nova Scotia, Canada.

SO TRANSPLANTATION, **(1995 Jul 15)** 60 (1) 71-6.
Journal code: 0132144. ISSN: 0041-1337.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199508

ED Entered STN: 19950911
Last Updated on STN: 19950911
Entered Medline: 19950831

AB In this study, we investigated the effects of treatment with **monoclonal antibodies** against the VLA-4 and LFA-1 adhesion molecules on rat islet allograft rejection. TA-2 and TA-3 are

function-blocking **mAb** against rat VLA-4 and LFA-1, respectively. Lewis rats were made diabetic (plasma glucose levels > 22.2 mmol/L) with streptozotocin. One week later, 1500 freshly isolated Wistar Furth rat islets were transplanted under the left kidney capsule of each rat. **Monoclonal antibodies** were administered intravenously at a dosage of 2 mg on the day of islet transplantation and then intraperitoneally every second day for 3 weeks or until graft rejection. Plasma glucose levels were monitored at least 3 times a week and blood leukocyte counts were monitored every 4 days. Rejection was defined as 2 plasma glucose levels > 11.1 mmol/L. Mean graft survival times in untreated and control **mAb**-treated rats were 5.3 and 6.0 days, respectively. Treatment with anti-VLA-4 or anti-LFA-1 resulted in only modest prolongation of mean graft survival time (9.3 and 7.4 days, respectively). However, treatment with the combination of anti-VLA-4 plus anti-LFA-1 resulted in long-term (i.e., 60-day) graft survival in 5 of 7 rats. Graft nephrectomy and histology confirmed islet graft survival at 60 days. A second Wistar Furth rat islet graft under the opposite renal capsule after graft nephrectomy did not show full tolerance; however, the function of the second graft was significantly prolonged without any immunosuppression. Combined blockade of VLA-4 and LFA-1 also markedly prolonged islet graft survival when islets were transplanted via the portal vein. In conclusion, both VLA-4 and LFA-1 play a role in islet allograft rejection and blockade of both prevents or greatly delays graft rejection.

CT Check Tags: Animal; Male; Support, Non-U.S. Gov't
***Antibodies, Monoclonal: TU, therapeutic use**
Diabetes Mellitus, Experimental: SU, surgery
Graft Rejection: PC, prevention & control
*Graft Survival: DE, drug effects
Islets of Langerhans: PA, pathology
***Islets of Langerhans Transplantation**
***Lymphocyte Function-Associated Antigen-1: IM, immunology**
Rats
Rats, Inbred Lew
Rats, Wistar
***Receptors, Very Late Antigen: IM, immunology**
Transplantation, Homologous

CN 0 (**Antibodies, Monoclonal**); 0 (Lymphocyte Function-Associated Antigen-1); 0 (Receptors, Very Late Antigen)

L34 ANSWER 6 OF 17 MEDLINE
AN **95184773** MEDLINE
DN **95184773** PubMed ID: **7879120**
TI Multilayer coating of **islets** of **Langerhans**: in vitro studies on a new method for immunoisolation.
AU Tatarkiewicz K; Sitarek E; Sabat M; Orlowski T
CS Institute of Biocybernetics and Biomedical Engineering, Polish Academy of Sciences, Warsaw.
SO TRANSPLANTATION PROCEEDINGS, **(1995 Feb)** 27 (1) 617.
Journal code: 0243532. ISSN: 0041-1345.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199504
ED Entered STN: 19950419
Last Updated on STN: 19950419
Entered Medline: 19950405
CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
Capsules
*Cell Separation: MT, methods
Cell Survival
Cells, Cultured

Centrifugation, Zonal: MT, methods
Heparin
***Islets of Langerhans: CY, cytology**
Islets of Langerhans Transplantation
Protamines
Rats
Transplantation, Heterologous
RN **9005-49-6 (Heparin)**
CN 0 (Capsules); 0 (Protamines)

L34 ANSWER 7 OF 17 MEDLINE
AN **95184663** MEDLINE
DN **95184663** PubMed ID: **7879025**
TI Potent immunosuppressive effect of anti-LFA-1 **monoclonal antibody** on islet allograft rejection.
AU Nishihara M; Gotoh M; Fukuzaki T; Ohta Y; Monden M; Yagita H; Okumura K; Miyasaka M; Mori T
CS Department of Surgery II, Osaka University Medical School, Japan.
SO TRANSPLANTATION PROCEEDINGS, **(1995 Feb)** 27 (1) 372.
Journal code: 0243532. ISSN: 0041-1345.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199504
ED Entered STN: 19950419
Last Updated on STN: 19950419
Entered Medline: 19950405
CT Check Tags: Animal; Male; Support, Non-U.S. Gov't
***Antibodies, Monoclonal: TU, therapeutic use**
Blood Glucose: ME, metabolism
Diabetes Mellitus, Experimental: BL, blood
Diabetes Mellitus, Experimental: TH, therapy
*Graft Rejection: PC, prevention & control
Graft Rejection: TH, therapy
Hyperglycemia
*Immunosuppressive Agents: TU, therapeutic use
***Islets of Langerhans Transplantation: IM, immunology**
Islets of Langerhans Transplantation: PH, physiology
***Lymphocyte Function-Associated Antigen-1: IM, immunology**
Mice
Mice, Inbred BALB C
Mice, Inbred C57BL
Rats
Transplantation, Homologous
CN 0 (**Antibodies, Monoclonal**); 0 (Blood Glucose); 0 (Immunosuppressive Agents); 0 (Lymphocyte Function-Associated Antigen-1)

L34 ANSWER 8 OF 17 MEDLINE
AN **95134104** MEDLINE
DN **95134104** PubMed ID: **7832654**
TI In vitro and in vivo evaluation of protamine-**heparin** membrane for microencapsulation of rat **Langerhans islets.**
AU Tatarkiewicz K; Sitarek E; Fiedor P; Sabat M; Orlowski T
CS Institute of Biocybernetics and Biomedical Engineering, Polish Academy of Sciences, Warsaw.
SO ARTIFICIAL ORGANS, **(1994 Oct)** 18 (10) 736-9.
Journal code: 7802778. ISSN: 0160-564X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199502

ED Entered STN: 19950307
Last Updated on STN: 19950307
Entered Medline: 19950223

AB Rat **pancreatic islets** were microencapsulated with multilayer protamine-**heparin** (PH) membrane. Basal and stimulatory insulin secretion of microencapsulated **islets** was similar to the controlled free **islets** in vitro. During the long-term culture (up to 2 weeks) mean insulin release of encapsulated **islets** did not significantly differ from the mean of free ones (the ratio of mentioned means was 54-167%). Empty PH microcapsules transplanted into Wistar rats intraperitoneally and under the kidney capsule were generally harmless up to 4 months. In only a few cases traces of fibrotic tissue around capsules entrapped in the omentum were found. No damage of microcapsules structure was observed. The worst results were obtained in the instance of retroperitoneal transplantation. We conclude, therefore, that PH membrane was proved to be highly biocompatible, nontoxic for **islets**, and did not impair viability and glucose-dependent insulin secretion of **Langerhans islets** in in vitro culture.

CT Check Tags: Animal; Male; Support, Non-U.S. Gov't
Biocompatible Materials
Cells, Cultured
Heparin
Insulin: SE, secretion
Islets of Langerhans: CY, cytology
Islets of Langerhans: SE, secretion
***Islets of Langerhans Transplantation**
*Membranes, Artificial
Protamines
Rats
Rats, Wistar

RN 11061-68-0 (Insulin); **9005-49-6 (Heparin)**
CN 0 (Biocompatible Materials); 0 (Protamines)

L34 ANSWER 9 OF 17 MEDLINE
AN **95121104** MEDLINE
DN **95121104** PubMed ID: **7821120**
TI Immunomodulation of transplant rejection using **monoclonal antibodies** and soluble receptors.
AU Alegre M L; Lenschow D J; Bluestone J A
CS Department of Pathology, University of Chicago, Illinois 60637.
SO DIGESTIVE DISEASES AND SCIENCES, **(1995 Jan)** 40 (1) 58-64. Ref: 40
Journal code: 7902782. ISSN: 0163-2116.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199502
ED Entered STN: 19950223
Last Updated on STN: 19950223
Entered Medline: 19950214

AB The main objective of our studies has been to optimize the effects of **monoclonal antibodies** (**MAbs**) and other immunosuppressive reagents to enhance organ graft survival. One such agent is OKT3, a **MAb** that is directed against the CD3 component of the human T-cell receptor (TCR) complex. Treatment of a rejection episode with OKT3 results in a rapid and efficient clearing of circulating T cells and reversal of most rejection episodes. Its wider use in transplantation and in the treatment of immune-mediated disease is limited by adverse reactions that follow the initial dose, the production of neutralizing

Abs, and the transient nature of the immunosuppression. We have engineered CDR-grafted "humanized" anti-CD3 **MAbs** that lack **Fc** -receptor binding activity through mutagenesis of amino acids in the **Fc** portion of the **MAb**. This results in an immunosuppressive anti-CD3 **MAb** that is less antigenic and one that does not induce the first-dose side effects. In addition, we have pursued a goal of developing a therapy that will induce donor-specific tolerance while maintaining overall recipient immune competency. Because antigen-specific T-cell activation depends not only on TCR-ligand interaction, but also on additional costimulatory signals mediated by accessory molecules such as CD28, blocking the binding of CD28 on T cells to its ligand B7, during TCR engagement, might modulate transplantation responses. Using a soluble fusion protein of human CTLA4, CTLA4-Ig, that binds B7 with high affinity, inhibition of human **pancreatic islet** rejection that occurs, at least in part, by affecting T-cell recognition of human B7+ antigen-presenting cells has been demonstrated.(ABSTRACT TRUNCATED AT 250 WORDS)

CT Check Tags: Human
Antibodies, Monoclonal: IM, immunology
***Antibodies, Monoclonal: TU, therapeutic use**
Graft Rejection: IM, immunology
*Graft Rejection: TH, therapy
*Immunosuppressive Agents: TU, therapeutic use
***Liver Transplantation**
Muromonab-CD3: TU, therapeutic use
*Receptors, Antigen, T-Cell: ME, metabolism

CN 0 (**Antibodies, Monoclonal**); 0 (Immunosuppressive Agents); 0 (Muromonab-CD3); 0 (Receptors, Antigen, T-Cell)

L34 ANSWER 10 OF 17 MEDLINE
AN **95090878** MEDLINE
DN **95090878** PubMed ID: **7998252**
TI Protamine-**heparin** membrane for cell microencapsulation.
AU Tatarkiewicz K; Sitarek E; Fiedor P; Sabat M; Orlowski T
CS Institute of Biocybernetics and Biomedical Engineering, Warsaw, Poland.
SO TRANSPLANTATION PROCEEDINGS, **(1994 Dec)** 26 (6) 3509.
Journal code: 0243532. ISSN: 0041-1345.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199501
ED Entered STN: 19950126
Last Updated on STN: 19950126
Entered Medline: 19950118

CT Check Tags: Animal; Support, Non-U.S. Gov't
Blood Glucose: ME, metabolism
Capsules
Cell Survival
***Cell Transplantation: MT, methods**
Cells, Cultured
Diabetes Mellitus, Experimental: BL, blood
*Diabetes Mellitus, Experimental: TH, therapy
Glucose: PD, pharmacology
Graft Rejection
Heparin
***Islets of Langerhans: CY, cytology**
Islets of Langerhans: DE, drug effects
Islets of Langerhans: SE, secretion
***Islets of Langerhans Transplantation: MT, methods**
Islets of Langerhans Transplantation: PH, physiology
Mice
Mice, Inbred BALB C

Polyethyleneimine
Protamines
Rats
Rats, Wistar
***Transplantation, Heterologous: MT, methods**
Transplantation, Heterologous: PH, physiology
RN 50-99-7 (Glucose); 9002-98-6 (Polyethyleneimine); **9005-49-6 (Heparin)**
CN 0 (Blood Glucose); 0 (Capsules); 0 (Protamines); 0 (protamine-**heparin** membrane)

L34 ANSWER 11 OF 17 MEDLINE
AN **95090770** MEDLINE
DN **95090770** PubMed ID: **7998156**
TI Treatment with anti-VLA-4 and LFA-1 **monoclonal antibodies** prolongs intraportal rat islet allograft survival.
AU Yang H; Issekutz T B; Wright J R Jr
CS Department of Pathology, Izaak Walton Killam Children's Hospital, Halifax, Nova Scotia, Canada.
SO TRANSPLANTATION PROCEEDINGS, **(1994 Dec)** 26 (6) 3325-6.
Journal code: 0243532. ISSN: 0041-1345.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199501
ED Entered STN: 19950126
Last Updated on STN: 19950126
Entered Medline: 19950118
CT Check Tags: Animal; Male; Support, Non-U.S. Gov't
***Antibodies, Monoclonal: PD, pharmacology**
Diabetes Mellitus, Experimental: PA, pathology
*Diabetes Mellitus, Experimental: TH, therapy
*Graft Survival: PH, physiology
Immunosuppression: MT, methods
Islets of Langerhans Transplantation: IM, immunology
Islets of Langerhans Transplantation: PA, pathology
***Islets of Langerhans Transplantation: PH, physiology**
***Lymphocyte Function-Associated Antigen-1: IM, immunology**
Portal System
Rats
Rats, Inbred Lew
Rats, Inbred WF
***Receptors, Very Late Antigen: IM, immunology**
Transplantation, Heterotopic
Transplantation, Homologous
CN 0 (**Antibodies, Monoclonal**); 0 (Lymphocyte Function-Associated Antigen-1); 0 (Receptors, Very Late Antigen)

L34 ANSWER 12 OF 17 MEDLINE
AN **94225606** MEDLINE
DN **94225606** PubMed ID: **8171670**
TI Successful rat-to-mouse xenotransplantation of **Langerhans islets** microencapsulated within a protamine-**heparin** membrane.
AU Tatarkiewicz K; Sitarek E; Fiedor P; Sabat M; Morzycka-Michalik M; Orlowski T
CS Institute of Biocybernetics and Biomedical Engineering, Polish Academy of Sciences, Warsaw.
SO TRANSPLANTATION PROCEEDINGS, **(1994 Apr)** 26 (2) 807-8.
Journal code: 0243532. ISSN: 0041-1345.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS Priority Journals
EM 199406
ED Entered STN: 19940613
Last Updated on STN: 19970203
Entered Medline: 19940602
CT Check Tags: Animal; Comparative Study; Support, Non-U.S. Gov't
Alginates
Biocompatible Materials
Biological Markers: BL, blood
Blood Glucose: ME, metabolism
Capsules
Diabetes Mellitus, Experimental: BL, blood
*Diabetes Mellitus, Experimental: SU, surgery
Graft Rejection: DI, diagnosis
*Graft Rejection: IM, immunology
Heparin
Islets of Langerhans Transplantation: IM, immunology
***Islets of Langerhans Transplantation: MT, methods**
Mice
Mice, Inbred BALB C
Polyethyleneimine
Polylysine: AA, analogs & derivatives
Protamines
Rats
Rats, Wistar
Transplantation, Heterologous: IM, immunology
***Transplantation, Heterologous: MT, methods**
RN 25104-18-1 (Polylysine); 9002-98-6 (Polyethyleneimine); **9005-49-6 (Heparin)**
CN 0 (Alginates); 0 (Biocompatible Materials); 0 (Biological Markers); 0 (Blood Glucose); 0 (Capsules); 0 (Protamines); 0 (alginate-polylysine-alginate); 0 (protamine-**heparin** membrane)

L34 ANSWER 13 OF 17 MEDLINE
AN **94225596** MEDLINE
DN **94225596** PubMed ID: **7513474**
TI Possible relationship between fibrotic overgrowth of alginate-polylysine-alginate microencapsulated **pancreatic islets** and the microcapsule integrity.
AU de Vos P; Wolters G H; van Schilfgaarde R
CS Surgical Research Laboratory, University of Groningen, The Netherlands.
SO TRANSPLANTATION PROCEEDINGS, **(1994 Apr)** 26 (2) 782-3.
Journal code: 0243532. ISSN: 0041-1345.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199406
ED Entered STN: 19940613
Last Updated on STN: 19970203
Entered Medline: 19940602
CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
*Alginates
Biocompatible Materials
Capsules
Dextrans
Fibrosis
***Islets of Langerhans Transplantation: MT, methods**
***Islets of Langerhans Transplantation: PA, pathology**
Membranes, Artificial
*Polylysine: AA, analogs & derivatives
Transplantation, Heterologous

Transplantation, Homologous
RN 25104-18-1 (Polylysine); 9004-54-0 (Dextrans); 9014-76-0 (sephadex)
CN 0 (Alginates); 0 (Biocompatible Materials); 0 (Capsules); 0 (alginate-polylysine-alginate)

L34 ANSWER 14 OF 17 MEDLINE
AN **94025055** MEDLINE
DN **94025055** PubMed ID: **8212148**
TI Human **islet** isolation--a prospective randomized comparison of **pancreatic** vascular perfusion with hyperosmolar citrate or University of Wisconsin solution.
AU Robertson G S; Chadwick D; Thirdborough S; Swift S; Davies J; James R; Bell P R; London N J
CS Department of Surgery, Leicester Royal Infirmary, United Kingdom.
SO TRANSPLANTATION, **(1993 Sep)** 56 (3) 550-3.
Journal code: 0132144. ISSN: 0041-1337.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 199310
ED Entered STN: 19940117
Last Updated on STN: 19970203
Entered Medline: 19931028
AB University of Wisconsin solution has become the most commonly used vascular perfusate during multiorgan donation world-wide. In the UK however, hyperosmolar citrate remains in common use. The purpose of this prospective randomized study was to compare the effect of systemic perfusion with UW or HOC on subsequent **islet** yield and purification for **pancreata** with short cold ischemic times. Seven **pancreata** were randomized to each group, with the donor age, **pancreas** weight, and period of cold ischemia being similar in both. Perfusion with UW was shown to inhibit collagenase digestion, and a higher concentration of this enzyme was needed to achieve comparable numbers of **islets** with good separation of exocrine and **islet** tissue after a similar period of digestion. There were no differences in the number, size, purity, or viability of **islets** between the two groups. In conclusion, UW solution offers no benefits over HOC for **pancreata** with short cold ischemic times, and because of its expense and need to use greater amounts of collagenase enzyme, we continue to use HOC.
CT Check Tags: Comparative Study; Human; Support, Non-U.S. Gov't
Adenosine
Allopurinol
Cell Survival
Citrates: CH, chemistry
Citric Acid
Cold: AE, adverse effects
Collagenases: ME, metabolism
Glutathione
Insulin
Ischemia: ET, etiology
***Islets of Langerhans**
Islets of Langerhans: CY, cytology
Osmolar Concentration
*Pancreas: BS, blood supply
Perfusion
Prospective Studies
Raffinose
Random Allocation
Tissue Donors

RN 11061-68-0 (Insulin); 315-30-0 (Allopurinol); 512-69-6 (Raffinose); 58-61-7 (Adenosine); 70-18-8 (Glutathione); 77-92-9 (Citric Acid)
CN 0 (Citrates); 0 (University of Wisconsin-lactobionate solution); EC 3.4.24.- (Collagenases)

L34 ANSWER 15 OF 17 MEDLINE
AN **93102412** MEDLINE
DN **93102412** PubMed ID: **1465972**
TI Xenograft acceptance by masking donor antigens.
AU Faustman D; Coe C
CS Immunobiology Laboratories, Massachusetts General Hospital East, Charlestown 02129.
SO TRANSPLANTATION PROCEEDINGS, **(1992 Dec)** 24 (6) 2854-5.
Journal code: 0243532. ISSN: 0041-1345.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199301
ED Entered STN: 19930205
Last Updated on STN: 19930205
Entered Medline: 19930115
CT Check Tags: Animal; Human
*Antigenic Modulation: IM, immunology
Graft Rejection: IM, immunology
*Graft Survival: IM, immunology
*Immunoglobulin Fragments: IM, immunology
***Islets of Langerhans Transplantation: IM, immunology**
Kidney
*Major Histocompatibility Complex: IM, immunology
Mice
Pilot Projects
Receptors, Antigen, T-Cell: IM, immunology
Receptors, Fc: IM, immunology
*T-Lymphocytes, Cytotoxic: IM, immunology
***Tissue Donors**
Transplantation, Heterologous
***Transplantation, Heterotopic: IM, immunology**
CN 0 (Immunoglobulin Fragments); 0 (Receptors, Antigen, T-Cell); 0 (Receptors, **Fc**)

L34 ANSWER 16 OF 17 MEDLINE
AN **92358237** MEDLINE
DN **92358237** PubMed ID: **1323143**
TI Long-term survival of xenogeneic **pancreatic islet** grafts induced by CTLA4lg.
CM Comment in: Science. 1992 Aug 7;257(5071):751
AU Lenschow D J; Zeng Y; Thistlethwaite J R; Montag A; Brady W; Gibson M G; Linsley P S; Bluestone J A
CS Ben May Institute, University of Chicago, IL 60637.
NC AI29531 (NIAID)
R29 DK40092 (NIDDK)
SO SCIENCE, **(1992 Aug 7)** 257 (5071) 789-92.
Journal code: 0404511. ISSN: 0036-8075.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199209
ED Entered STN: 19920925
Last Updated on STN: 19970203
Entered Medline: 19920908
AB Antigen-specific T cell activation depends on T cell receptor-ligand

interaction and costimulatory signals generated when accessory molecules bind to their ligands, such as CD28 to the B7 (also called BB1) molecule. A soluble fusion protein of human CTLA-4 (a protein homologous to CD28) and the immunoglobulin (Ig) G1 **Fc** region (CTLA4Ig) binds to human and murine B7 with high avidity and blocks T cell activation in vitro. CTLA4Ig therapy blocked human **pancreatic islet** rejection in mice by directly affecting T cell recognition of B7+ antigen-presenting cells. In addition, CTLA4Ig induced long-term, donor-specific tolerance, which may have applications to human organ transplantation.

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Antibodies, Monoclonal: TU, therapeutic use
Antigens, Differentiation: IM, immunology
*Antigens, Differentiation: TU, therapeutic use
*Diabetes Mellitus, Experimental: SU, surgery
*Graft Survival: IM, immunology
Graft Survival: PH, physiology
Immunoglobulin G
Immunoglobulins, Fc
*Immunosuppressive Agents: TU, therapeutic use
***Islets of Langerhans Transplantation: IM, immunology**
Islets of Langerhans Transplantation: PH, physiology
Mice
Mice, Inbred Strains
Phosphates: AN, analysis
*Phosphates: ME, metabolism
Receptors, Cell Surface: IM, immunology
*Recombinant Fusion Proteins: TU, therapeutic use
Time Factors
***Transplantation, Heterologous: IM, immunology**
Transplantation, Heterologous: PH, physiology
Uranium: AN, analysis
*Uranium: ME, metabolism

RN 18433-48-2 (hydrogen uranyl phosphate); 7440-61-1 (Uranium)

CN 0 (**Antibodies, Monoclonal**); 0 (Antigens, Differentiation); 0 (CTLA-4); 0 (Immunoglobulin G); 0 (Immunoglobulins, **Fc**); 0 (Immunosuppressive Agents); 0 (Phosphates); 0 (Receptors, Cell Surface); 0 (Recombinant Fusion Proteins)

L34 ANSWER 17 OF 17 MEDLINE

AN **91262652** MEDLINE

DN **91262652** PubMed ID: **1710828**

TI Prevention of xenograft rejection by masking donor HLA class I antigens.

AU Faustman D; Coe C

CS Diabetes Unit, Massachusetts General Hospital, Harvard Medical School, Boston 02129.

SO SCIENCE, **(1991 Jun 21)** 252 (5013) 1700-2.
Journal code: 0404511. ISSN: 0036-8075.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199107

ED Entered STN: 19910802
Last Updated on STN: 19960129
Entered Medline: 19910716

AB Destruction of target cells by cytotoxic T lymphocytes requires the presence of HLA (human lymphocyte antigen) class I antigens on the target cells for adhesion as well as for triggering of the antigen-specific T cell receptor. Rejection of xenogeneic human **pancreatic islets** and liver was circumvented by masking, before transplantation, donor antigens with F(ab')2 antibody fragments to HLA

class I or tissue-specific epitopes. This strategy eliminated the need for recipient immunosuppression and allowed **islet** xenograft survival beyond 200 days, as demonstrated functionally by C peptide secretion as well as by histology. These in vivo observations are consistent with the importance of donor HLA class I in eliciting graft rejection and have potential applicability to the successful transplantation of other HLA class I-bearing donor tissues.

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
Antibodies, Monoclonal: IM, immunology
Antigen-Antibody Complex
Antigens, CD: IM, immunology
Antigens, CD29
C-Peptide: BL, blood
*Graft Rejection
*Histocompatibility Antigens Class I: IM, immunology
Immunoglobulins, Fab: IM, immunology
***Islets of Langerhans: IM, immunology**
***Islets of Langerhans Transplantation: IM, immunology**
Mice
Mice, Inbred BALB C
*T-Lymphocytes: IM, immunology
Transplantation, Heterologous

CN 0 (**Antibodies, Monoclonal**); 0 (Antigen-Antibody Complex); 0 (Antigens, CD); 0 (Antigens, CD29); 0 (C-Peptide); 0 (Histocompatibility Antigens Class I); 0 (Immunoglobulins, Fab)

=> d all tot

L38 ANSWER 1 OF 11 MEDLINE
AN **2001136510** MEDLINE
DN **20544218** PubMed ID: **11095109**
TI Isolated human islets trigger an instant blood mediated inflammatory reaction: implications for intraportal islet transplantation as a treatment for patients with type 1 diabetes.
AU Bennet W; Groth C G; Larsson R; Nilsson B; Korsgren O
CS Department of Transplantation Surgery, Karolinska Institute, Huddinge Hospital, Sweden.
SO UPSALA JOURNAL OF MEDICAL SCIENCES, (2000) 105 (2) 125-33. Ref: 24
Journal code: 0332203. ISSN: 0300-9734.
CY Sweden
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200103
ED Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010301
AB **Islet** transplantation offers a logical means to treat insulin-dependent diabetes. However, for reasons poorly understood, the clinical results with **islet** transplantation have been vastly inferior to those obtained with whole organ **pancreas** transplantation. The conventional technique for transplanting isolated **islets** is by intraportal injection, with the **islets** being trapped in the liver. Human **islets** exposed to human blood trigged an "instant blood mediated inflammatory reaction", IBMIR, characterised by platelet consumption, and activation of the coagulation and complement systems. The **islets** became surrounded by clots and infiltrated with leukocytes, and there was evidence of **islet** damage as reflected in insulin dumping. When **heparin** and a complement inhibitor (SCRI), was added to the system, IBMIR was suppressed

and **islet** damage reduced. After intraportal pig-to-pig **islet** intraportal allotransplantation similar morphological changes was found, corroborating the in vitro findings. Thus, IBMIR inflicts a significant damage to human **islets** exposed to human blood and IBMIR will also, most likely, enhance the subsequent specific, cell mediated, rejection. Platelet and complement activation seem to be the most important factors in the pathogenesis of IBMIR. The results presented strongly suggest that IBMIR observed both in vitro and in vivo when isolated **islets** come in contact with blood could provide an explanation for the unsatisfactory results seen in clinical **islet** allotransplantation.

CT Check Tags: Human; Support, Non-U.S. Gov't
Blood Coagulation
Blood Platelets: PH, physiology
Complement Activation
*Diabetes Mellitus, Insulin-Dependent: TH, therapy
*Inflammation: ET, etiology
***Islets of Langerhans Transplantation**
Portal System
Transplantation, Homologous

L38 ANSWER 2 OF 11 MEDLINE
AN **2000216291** MEDLINE
DN **20216291** PubMed ID: **10755515**
TI Damage to porcine **islets** of **Langerhans** after exposure to human blood in vitro, or after intraportal transplantation to cynomologus monkeys: protective effects of sCR1 and **heparin**.
CM Comment in: Transplantation. 2000 Mar 15;69(5):708-9
AU Bennet W; Sundberg B; Lundgren T; Tibell A; Groth C G; Richards A; White D J; Elgue G; Larsson R; Nilsson B; Korsgren O
CS Department of Transplantation Surgery, Karolinska Institutet, Huddinge Hospital, Sweden.
SO TRANSPLANTATION, (2000 Mar 15) 69 (5) 711-9.
Journal code: 0132144. ISSN: 0041-1337.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200004
ED Entered STN: 20000427
Last Updated on STN: 20000427
Entered Medline: 20000419
AB BACKGROUND: Porcine **islets** offer an attractive alternative to human **islets** in clinical **islet** transplantation. The preferred method of **islet** transplantation is intra-portal injection into the liver. We have recently shown, both in vitro with human **islets** and in vivo with porcine **islets**, that **islets** exposed to allogeneic blood trigger an injurious inflammatory reaction characterized by activation of both coagulation and the complement systems. We have now tested whether a similar reaction is triggered when xenogeneic porcine **islets** are exposed to human blood in vitro and after intraportal transplantation into primates. Furthermore, we investigated the effect of inhibiting the complement and coagulation systems. METHOD: **Islets** isolated from adult and fetal porcine **pancreas** were perfused with fresh human blood in surface heparinized PVC tubings for 5-60 min. Blood cell counts and parameters related to coagulation and the complement system were analyzed, and **islets** were retrieved after the perifusion was examined by immunohistochemical method. **Heparin** and soluble complement receptor 1 (sCR1; TP10, 100 microg/ml) were added to the system in some experiments. Furthermore, adult porcine **islets** were transplanted intraportally into untreated and sCR1- (40 mg/kg BW i.v.) treated cynomolgus monkeys, and plasma insulin concentration was monitored during

60 min after transplantation. RESULTS: Porcine **islets** perifused with human blood triggered an immediate inflammatory reaction, characterized by a rapid consumption and activation of platelets, consumption of neutrophils and monocytes, activation of the coagulation and complement systems, and release of large amounts of insulin. **Islet** morphologic analysis revealed damaged **islets** embedded in clots and infiltrated with CD11+ leukocytes. C3a and C5b-9 was deposited on the **islet** surface, but human immunoglobulin was not. Complement inhibition with sCR1 reduced insulin release significantly. Intraportal **islet** transplantation into untreated cynomolgus monkeys resulted in a marked and rapid increase in plasma insulin concentration indicative of **islet** damage. Pretreatment of the monkeys with sCR1 resulted in significantly less insulin release than in untreated control monkeys. CONCLUSION: Exposure of isolated xenogeneic **islets** of **Langerhans** to blood, both in vitro and in vivo, resulted in acute **islet** damage. Complement and platelets seem to have a central role in the reactions described. Strategies to efficiently inhibit these reactions will be crucial for clinical intraportal **islet** xenotransplantation to be successful.

CT Check Tags: Animal; Human; In Vitro; Support, Non-U.S. Gov't
*Blood Physiology
Immunohistochemistry: MT, methods
Injections
Insulin: SE, secretion
Islets of Langerhans: ME, metabolism
Islets of Langerhans: PA, pathology
Islets of Langerhans: SE, secretion
***Islets of Langerhans Transplantation: MT, methods**
Macaca fascicularis
Perfusion
Portal System
Staining and Labeling
Swine
***Transplantation, Heterologous**

RN 11061-68-0 (Insulin)

L38 ANSWER 3 OF 11 MEDLINE
AN 1999440905 MEDLINE
DN 99440905 PubMed ID: 10512353
TI Incompatibility between human blood and isolated **islets** of **Langerhans**: a finding with implications for clinical intraportal **islet** transplantation?.
AU Bennet W; Sundberg B; Groth C G; Brendel M D; Brandhorst D; Brandhorst H; Bretzel R G; Elgue G; Larsson R; Nilsson B; Korsgren O
CS Department of Transplantation Surgery, Karolinska Institutet, Huddinge Hospital, Sweden.. william.bennet@transpl.hs.sll.se
SO DIABETES, **(1999 Oct)** 48 (10) 1907-14.
Journal code: 0372763. ISSN: 0012-1797.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199910
ED Entered STN: 19991101
Last Updated on STN: 19991101
Entered Medline: 19991019
AB The remarkable difference in success rates between clinical **pancreas** transplantation and **islet** transplantation is poorly understood. Despite the same histocompatibility barrier and similar immunosuppressive treatments in both transplantation procedures, human intraportal **islet** transplantation has a much inferior success rate than does vascularized **pancreas** transplantation. Thus far, little attention has been directed to the possibility that **islets**

transplanted into the blood stream may elicit an injurious incompatibility reaction. We have tested this hypothesis in vitro with human **islets** and in vivo with porcine **islets**. Human **islets** were exposed to nonanticoagulated human ABO-compatible blood in surface-heparinized polyvinyl chloride tubing loops. **Heparin** and/or the soluble complement receptor 1 (sCR1) TP10 were tested as additives. Adult porcine **islets** were transplanted intraportally into pigs, and the liver was recovered after 60 min for immunohistochemical staining. Human **islets** induced a rapid consumption and activation of platelets. Neutrophils and monocytes were also consumed, and the coagulation and complement systems were activated. Upon histological examination, **islets** were found to be embedded in clots and infiltrated with CD11+ leukocytes. Furthermore, the cellular morphology was disrupted. When **heparin** and sCR1 were added to the blood, these events were avoided. Porcine **islets** retrieved in liver biopsies after intraportal **islet** allotransplantation showed a morphology similar to that of human **islets** perifused in vitro. Thus, exposure of isolated **islets** of **Langerhans** to allogenic blood resulted in significant damage to the **islets**, a finding that could explain the unsatisfactory clinical results obtained with intraportal **islet** transplantation. Because administration of **heparin** in combination with a soluble complement receptor abrogated these events, such treatment would presumably improve the outcome of clinical **islet** transplantation by reducing both initial **islet** loss and subsequent specific immune responses.

CT Check Tags: Animal; Female; Human; Male; Support, Non-U.S. Gov't
Adult
*Blood: IM, immunology
Enzyme-Linked Immunosorbent Assay
*Inflammation: ET, etiology
Inflammation: IM, immunology
Insulin: ME, metabolism
***Islets of Langerhans: IM, immunology**
Islets of Langerhans: ME, metabolism
***Islets of Langerhans Transplantation: AE, adverse effects**
Islets of Langerhans Transplantation: IM, immunology
Leukocyte Count
Middle Age
Platelet Count
Portal Vein
Rabbits
Swine

RN 11061-68-0 (Insulin)

L38 ANSWER 4 OF 11 MEDLINE
AN 1999086674 MEDLINE
DN 99086674 PubMed ID: 9869850
TI Reversal of hyperglycemia in streptozotocin diabetic mice by xenotransplantation of microencapsulated rat islets.
AU Tatarkiewicz K; Sitarek E; Sabat M; Orlowski T
CS Institute of Biocybernetics & Biomedical Engineering, Warsaw, Poland.
SO ANNALS OF TRANSPLANTATION, **(1997)** 2 (2) 20-3.
Journal code: 9802544. ISSN: 1425-9524.
CY Poland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199902
ED Entered STN: 19990216
Last Updated on STN: 19990216
Entered Medline: 19990202
AB Rat **pancreatic islets** were immunoisolated within alginate capsules with additional polyethyleneimine-protamine-

heparin highly biocompatible membrane. Perifusion study in vitro demonstrated satisfactory similarities between the insulin release profiles of encapsulated and free **islets**. Concordant xenotransplantation of microencapsulated rat **islets** significantly prolonged mean time of restored normoglycemia (46 +/- 15 days) in streptozotocin-diabetic BALB/c mice recipients comparing to uncoated grafts (7 +/- 2 days).

CT Check Tags: Animal; Male; Support, Non-U.S. Gov't
Alginates
Blood Glucose: ME, metabolism
*Diabetes Mellitus, Experimental: SU, surgery
Heparin
*Hyperglycemia: SU, surgery
***Islets of Langerhans Transplantation**
Mice
Mice, Inbred BALB C
Microspheres
*Pancreas, Artificial
Polyethyleneimine
Polymers
Protamines
Rats
***Transplantation, Heterologous**

RN 9002-98-6 (Polyethyleneimine); 9005-32-7 (alginic acid); **9005-49-6 (Heparin)**

CN 0 (Alginates); 0 (Blood Glucose); 0 (Polymers); 0 (Protamines)

L38 ANSWER 5 OF 11 MEDLINE
AN 96257665 MEDLINE
DN 96257665 PubMed ID: 8658913
TI Unpurified islet cell transplantation in diabetic rats.
AU Nomura Y; Ito S; Ichikawa N; Meigata K; Kikuchi K; Ando Y; Watanabe K; Degawa H; Beck Y; Tomikawa S; Nagao T; Uchida H
CS Department of Surgery and Organ Transplantation, University of Tokyo, Japan.
SO TRANSPLANTATION PROCEEDINGS, **(1996 Jun)** 28 (3) 1849-50.
Journal code: 0243532. ISSN: 0041-1345.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199608
ED Entered STN: 19960808
Last Updated on STN: 19960808
Entered Medline: 19960801

CT Check Tags: Animal; Male
*Anticoagulants: PD, pharmacology
Antithrombin III: PD, pharmacology
*Blood Pressure: DE, drug effects
Diabetes Mellitus, Experimental: SU, surgery
Gabexate: PD, pharmacology
*Graft Survival: DE, drug effects
Heparin: PD, pharmacology
***Islets of Langerhans Transplantation: MT, methods**
Islets of Langerhans Transplantation: PH, physiology
Portal Vein: DE, drug effects
*Portal Vein: PH, physiology
Rats
Rats, Wistar
Transplantation, Isogeneic

RN 39492-01-8 (Gabexate); 9000-94-6 (Antithrombin III); **9005-49-6 (Heparin)**

CN 0 (Anticoagulants)

L38 ANSWER 6 OF 11 MEDLINE
AN 96024684 MEDLINE
DN 96024684 PubMed ID: 7573524
TI Selective binding of platelet factor 4 to regions of active angiogenesis in vivo.
AU Hansell P; Maione T E; Borgstrom P
CS La Jolla Institute for Experimental Medicine, California 92037, USA.
SO AMERICAN JOURNAL OF PHYSIOLOGY, **(1995 Sep)** 269 (3 Pt 2) H829-36.
Journal code: 0370511. ISSN: 0002-9513.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199511
ED Entered STN: 19951227
Last Updated on STN: 19951227
Entered Medline: 19951102
AB In a previous study we suggested that recombinant human platelet factor 4 (rhPF4) preferentially binds in vivo to regions of active angiogenesis/endothelial cell migration. To test this hypothesis, binding of fluorescently labeled rhPF4 to newly formed vessels was compared with that of the normal skin vasculature, using syngeneic **Langerhans islets** as inducers of angiogenesis. **Islets** were implanted in the dorsal skinfold chamber of the hamster, and the binding of rhPF4 was studied using intravital fluorescence microscopy. Intra-arterially injected rhPF4 labeled, with high intensity, the endothelium along newly formed vessels of the **islets** (1,632 +/- 617 microns labeled vessel length per **islet**), and only on rare occasions (1 +/- 2 sites per cm2 skinfold) were short (62 +/- 48 microns) intense-labeled sites found in the normal vasculature of the skinfold. **Heparin** could displace most of the label if injected within 10 min after the rhPF4 injection, but not 30 min after. In conclusion, rhPF4-preferentially binds to regions of active angiogenesis in vivo. On binding, rhPF4 is internalized as judged from a decreasing **heparin** sensitivity with time after rhPF4 injection. The infrequent rhPF4-labeling sites in the normal skin vasculature most likely represent regions of newly formed cells/migration, i.e., normal endothelial turnover, supporting our previous findings demonstrating that the occurrence of such regions is rare in the normal microvasculature. Furthermore, despite the previously demonstrated short half-life in plasma, systemically injected rhPF4 will target regions of angiogenesis with high affinity, thereby facilitating the antiangiogenic effect of PF4.
CT Check Tags: Animal; Human; Male; Support, Non-U.S. Gov't
Fluorescein-5-isothiocyanate
Hamsters
Heparin: PD, pharmacology
Islets of Langerhans: BS, blood supply
Islets of Langerhans Transplantation
Mesocricetus
Microscopy, Fluorescence
*Neovascularization, Physiologic: PH, physiology
*Platelet Factor 4: ME, metabolism
Recombinant Proteins: ME, metabolism
Skin: BS, blood supply
Skin: SU, surgery
RN 3326-32-7 (Fluorescein-5-isothiocyanate); 37270-94-3 (Platelet Factor 4); **9005-49-6 (Heparin)**
CN 0 (Recombinant Proteins)

L38 ANSWER 7 OF 11 MEDLINE
AN 93091097 MEDLINE
DN 93091097 PubMed ID: 1457692

TI Hybrid artificial **pancreas**: **islet** transplantation inside membrane bioreactors.
AU Lombardi C P; Urso A; Careddu G; Ghirlanda G; Catapano G; Brisinda G; Ceriati F; Bellantone R; Doglietto G B; Crucitti F
CS Chair of Surgical Pathology, Catholic University, Rome, Italy.
SO BIOMATERIALS, ARTIFICIAL CELLS, AND IMMOBILIZATION BIOTECHNOLOGY, **(1992)** 20 (5) 1177-92.
Journal code: 9111988. ISSN: 1055-7172.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199301
ED Entered STN: 19930129
Last Updated on STN: 19930129
Entered Medline: 19930114
AB The use of **pancreatic islet** transplantation in membrane bioreactors put in vascular circuits aims at resetting the glucose homeostasis in diabetic or **pancreatectomized** patients, avoiding immune host rejection. Our experience was carried out at following stages: porcine **pancreas** explantation and enzymatic separation of endocrine tissue from exocrine fraction by collagenase; evaluation of **islet** functionality (culture tests); in vitro tests of the **islets**-bioreactor system, to assess the metabolic response to the glucose; in vivo evaluation to assay the haemodynamic behaviour. The trials showed a good metabolic bioreactor functionality and a decreasing incidence of coagulative problems.
CT Check Tags: Animal; Female
Glucose: ME, metabolism
Heparin
Insulin: SE, secretion
***Islets of Langerhans Transplantation: MT, methods**
Membranes, Artificial
Swine
RN 11061-68-0 (Insulin); 50-99-7 (Glucose); **9005-49-6 (Heparin)**

L38 ANSWER 8 OF 11 MEDLINE
AN 92314603 MEDLINE
DN 92314603 PubMed ID: 1377558
TI Induction of angiogenesis by growth factors: relevance to **pancreatic islet** transplantation.
AU Stagner J I; Samols E
CS Veterans Administration Medical Center, Louisville, KY.
SO EXS, **(1992)** 61 381-5.
Journal code: 9204529.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199208
ED Entered STN: 19920815
Last Updated on STN: 19960129
Entered Medline: 19920806
AB Biodegradable pellets releasing 20 ng/day of endothelial cell growth factor alpha (alpha ECGF) or a- or b-fibroblast growth factor (FGF) and 90 micrograms/day of **heparin** were implanted beneath the renal capsule in rats and dogs and the muscularis/serosal border of the pyloric stomach in dogs to test for angiogenesis in a potential **pancreatic islet** transplant site. These factors were also tested in vitro to determine whether the capillary bed of the isolated **islet** could be preserved. alpha ECGF was superior to a- or bFGF in promoting endothelial cell growth and capillary formation in isolated **islets** . Both a- or bFGF and alpha ECGF induced the development of a dense

capillary bed in the dog stomach, whereas in the kidney site alpha ECGF was more effective in the rat than was a- or bFGF. Priming the isolated **islet** as well as the transplant site prior to **islet** transplantation resulted in **islet** blood flow being established within 3 days in contrast to 7-14 days in controls.

CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.
Capillaries: DE, drug effects
Capillaries: PH, physiology
Cells, Cultured
Dipyridamole: PD, pharmacology
Dogs
*Endothelial Growth Factors: PD, pharmacology
*Fibroblast Growth Factor 1: PD, pharmacology
*Fibroblast Growth Factor 2: PD, pharmacology
***Islets of Langerhans: BS, blood supply**
***Islets of Langerhans Transplantation: PH, physiology**
*Neovascularization, Pathologic
Rats
Regional Blood Flow: DE, drug effects
Transplantation, Heterologous

RN 103107-01-3 (Fibroblast Growth Factor 2); 104781-85-3 (Fibroblast Growth Factor 1); 58-32-2 (Dipyridamole)

CN 0 (Endothelial Growth Factors)

L38 ANSWER 9 OF 11 MEDLINE

AN 92087504 MEDLINE

DN 92087504 PubMed ID: 1750208

TI [Stable reduction of endogenous insulin production in the body in experimental insulin-dependent diabetes].
Ustoichivoe vosstanovlenie produktsii endogennogo insulina v organizme pri eksperimental'nom insulinzavisimom diabete.

AU Kudriashov B A; Ul'ianov A M

SO VOPROSY MEDITSINSKOI KHIMII, **(1991 Jul-Aug)** 37 (4) 40-3.
Journal code: 0416601. ISSN: 0042-8809.

CY USSR

DT Journal; Article; (JOURNAL ARTICLE)

LA Russian

FS Priority Journals

EM 199201

ED Entered STN: 19920209
Last Updated on STN: 19920209
Entered Medline: 19920121

AB Implantation of beta-cells allogenic culture into animals with alloxan diabetes did not produce persistent positive effect. The implanted beta-cells lost their viability as a result of toxic effect of natural diabetogenic factor occurring in blood plasma during insulin-dependent diabetes. Long-term administration of **heparin** into these animals within first 90 days of the experiment enabled to avoid the negative phenomenon and to neutralize the diabetogenic factor activity. Under these conditions the implanted beta-cells effectively produced endogenous insulin and the symptoms of diabetes disappeared within 14 months.

CT Check Tags: Animal; Male
Alloxan: PD, pharmacology
Blood Glucose: AN, analysis
*Diabetes Mellitus, Experimental: ME, metabolism
English Abstract
*Insulin: BI, biosynthesis
Islets of Langerhans Transplantation
Pituitary Hormones: BL, blood
Rats

RN 11061-68-0 (Insulin); 50-71-5 (Alloxan)

CN 0 (Blood Glucose); 0 (Pituitary Hormones); 0 (diabetogenic protein)

L38 ANSWER 10 OF 11 MEDLINE
AN 87044406 MEDLINE
DN 87044406 PubMed ID: 2877528
TI [Surgical experiences with segmental pancreatic transplantation in type I diabetes].
Chirurgische Erfahrungen mit der segmentalen Pankreastransplantation bei Typ I Diabetikern.
AU Abendroth D; Illner W D; Land W
SO ZEITSCHRIFT FUR EXPERIMENTELLE CHIRURGIE, TRANSPLANTATION, UND KUNSTLICHE ORGANE, **(1986)** 19 (4) 234-6.
Journal code: 8302880. ISSN: 0232-7295.
CY GERMANY, EAST: German Democratic Republic
DT Journal; Article; (JOURNAL ARTICLE)
LA German
FS Priority Journals
EM 198611
ED Entered STN: 19900302
Last Updated on STN: 19950206
Entered Medline: 19861128
CT Check Tags: Human
Antibiotics: TU, therapeutic use
*Diabetes Mellitus, Insulin-Dependent: TH, therapy
Follow-Up Studies
Heparin: TU, therapeutic use
Insulin: TU, therapeutic use
***Islets of Langerhans Transplantation**
Somatostatin: TU, therapeutic use
RN 11061-68-0 (Insulin); 51110-01-1 (Somatostatin); **9005-49-6 (Heparin)**
CN 0 (Antibiotics)

L38 ANSWER 11 OF 11 MEDLINE
AN 77044312 MEDLINE
DN 77044312 PubMed ID: 791227
TI Studies with the autotransplanted ovine pancreas: glucagon and insulin secretion.
AU Arcus A C; Ellis M J; Kirk R D; Beaven D W; Donald R A; Hart D S; Holland G W; Redekopp C
SO AUSTRALIAN JOURNAL OF BIOLOGICAL SCIENCES, **(1976 Jul)** 29 (3) 223-36.
Journal code: 0370613. ISSN: 0004-9417.
CY Australia
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197612
ED Entered STN: 19900313
Last Updated on STN: 19900313
Entered Medline: 19761223
AB Basic studies on the secretion of glucagon and insulin by the ovine pancreatic autotransplant in the neck are described. Of the 17 transplants in the series none failed to secrete glucagon and only three failed to secrete insulin in detectable amounts. The longest surviving transplant actively secreted both hormones 3 years after transplantation and five other transplants were functional and the animals healthy after 16 months. Exocrine secretion disappears shortly after transplantation. Sodium butyrate and alanine each promoted the secretion of both hormones by the transplant. Glucagon failed to promote insulin secretion by the transplant, although it apparently stimulated the ovine in situ pancreas. The immediate (presumably direct) effect of insulin was to inhibit transplant glucagon secretion. Hypoglycaemia induced by peripheral insulin administration failed to stimulate glucagon secretion by the transplant,

although it did promote glucagon secretion by the ovine in situ pancreas. **Heparin** did not markedly suppress basal transplant secretion of either glucagon or insulin. Phasic response patterns occurred with both hormones during long butyrate perfusions, although first-phase responsiveness was not a constant feature. In one trial, first-phase responses fell off with repeated short butyrate infusions. Glucagon and insulin secretory patterns in response to butyrate were remarkably alike, suggesting a common mechanism. Loss of specific functions by the ovine pancreas after transplantation is discussed.

CT Check Tags: Animal; Female
Arginine: PD, pharmacology
Butyrates: PD, pharmacology
Dose-Response Relationship, Drug
Glucagon: PD, pharmacology
*Glucagon: SE, secretion
Heparin: PD, pharmacology
Insulin: PD, pharmacology
*Insulin: SE, secretion
***Islets of Langerhans: SE, secretion**
***Pancreas Transplantation**
Secretory Rate: DE, drug effects
*Sheep: PH, physiology
Stimulation, Chemical
Transplantation, Autologous

RN 11061-68-0 (Insulin); 74-79-3 (Arginine); **9005-49-6 (Heparin);** 9007-92-5 (Glucagon)

CN 0 (Butyrates)

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(FILE 'MEDLINE' ENTERED AT 13:06:20 ON 18 DEC 2002)

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                DEL HIS
                E ISLET/CT
                E E24+ALL
L1          4277 S E8+NT
                E ISLET/CT
                E E23+ALL
L2         22706 S E12+NT
                E TRANSPLANTATION/CT
                E E3+ALL
L3        256333 S E3+NT
L4        135197 S E45+NT OR E46+NT OR E47+NT OR 348+NT OR E49+NT
L5          4759 S L3,L4 AND L1,L2
L6          4759 S L1,L5
L7          5008 S ISLET(L)(LANGERHAN? OR PANCREA?) AND L3,L4
L8          5008 S L6,L7
L9            18 S L8 AND HEPARIN
L10            2 S L8 AND RGD
L11            4 S L8 AND (ARG OR ARGIN?)()(GLY OR GLYC?)()(ASP OR ASPART?)
L12            0 S L8 AND ARGINYLGLYCYLASPART?
L13           63 S L8 AND MAB
L14          269 S L8 AND MONOCLON?(L)ANTIBOD?
                E MONOCLONAL ANTIBODY/CT
                E E1+ALL
                E E2+ALL
L15          217 S L8 AND E8+NT
                E PLATELET INTEGRIN/CT
                E INTEGRIN/CT
L16           28 S L8 AND E3-E96
L17            2 S L8 AND E97-E142
                E E143+ALL
L18           34 S L8 AND E13+NT
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L19          27 S L8 AND FC?
                E FC RECEPTOR/CT
                E E4+ALL
                E E2+ALL
L20           5 S L8 AND E13+NT
L21           1 S L8 AND THROMBIN(L)ANTITHROMBIN
L22           5 S L8 AND ANTICOAGUL?
                E ANTICOAGULANT/CT
                E E8+ALL
L23          31 S L8 AND E7+NT
L24         101 S L9-L11,L16-L23
L25          30 S L13,L14 AND L24
L26         101 S L24,L25
L27          74 S L26 AND PY<=1999
L28          27 S L27 NOT AB/FA
L29          72 S L27/ENG
L30          16 S L29/HUMAN
                SEL DN AN 3 7 8 11-15
L31           8 S L30 AND E1-E24
L32          56 S L29 NOT L30
                SEL DN AN 11 13 27 28 30 31 32 33 38
L33           9 S E25-E51
L34          17 S L31,L33 AND L1-L33

     FILE 'MEDLINE' ENTERED AT 13:43:29 ON 18 DEC 2002
L35          12 S L9 NOT L34
L36           9 S L35 AND PY<=1999
                SEL L35 DN AN 2 3
L37           2 S E52-E57 AND L35
L38          11 S L36,L37
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